

Applicants acknowledge that methods of sterile filtration, lyophilization of aqueous acetic acid solutions of peptides and the manufacture of lyophilizates of medicaments are generally known in the art. However, it is not possible to conclude, solely by consideration of the cited art, that by solubilizing a gel-forming peptide in acetic acid, a sterile filterable solution can be manufactured. As persons of skill in the art are aware, the gel-forming properties of a peptide are caused by interaction between molecules. These interactions can arise by hydrophobic centers whereby electrostatically loaded groups can act against one another. Therefore, the gel-forming properties depend very strongly on the chemical structure of the peptide and cannot be reliably predicted. Furthermore, the gel-formation depends on additional factors, for example, on the concentration of the solution and time allowed. In addition, gel-formation is strongly increased by a number of further ions such as Cl^- , SO_4^- , PO_4^- etc., resulting in a precipitation of the peptide. In such instances, a sterile filtration is impossible.

Furthermore, the present invention is not comparable with the objective of U.S. Patent No. 5,204,335 (Sauerbier) wherein the described substance is not a peptide and shows no gel-forming properties. Thus, a person of skill in the art would not have been motivated to combine this reference with any of the other cited references in order to achieve the presently claimed invention. Isosfamide is a substance of the class of

nitrogeniosts used for cancer chemotherapy and is not related to the decapeptide cetrorelix. The Examiner's comment that "Sauerbier et al. teach the lyophilization of a product for use and that this peptide had been sterilized" is not understood. Clarification is requested.

Callahan (US 4,908,475) has isolated heptapeptides which are also different from cetrorelix and do not exhibit the problem of gel formation. In addition, the objective of Callahan was not the production of a sterile filtered medicament for injection purposes, but only the isolation and purification of the peptide, as detailed in the Amendment filed April 20, 1998.

In summary, Applicants respectfully submit that in view of the great structural differences between synthetic peptides, which result in different chemical and physical properties, the combined references do not suggest to a skilled artisan how to prepare a sterile cetrorelix lyophilizate and the presently claimed invention is novel and unobvious. Withdrawal of the § 103 rejection is respectfully requested.

All rejections having been addressed, it is submitted that this application is in condition for allowance. If the application is not considered to be in condition for

allowance, the Examiner is respectfully requested to telephone the undersigned to discuss any remaining issues.

Respectfully submitted,

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